

WHAT IS CLAIMED IS:

- sub 1
2 3
- 1 1. A mutant antibody comprising a reactive site not present in the wild-
2 type of said antibody and a complementarity-determining region that specifically binds to a
3 metal chelate, wherein said reactive site is in a position proximate to or within said
4 complementarity-determining region.
 - 1 2. The mutant antibody according to claim 1, wherein said reactive site is
2 a side-chain of a naturally occurring or non-naturally occurring amino acid.
 - 1 3. The mutant antibody according to claim 2, wherein said reactive site is
2 the -SH group of cysteine.
 - 1 4. An isolated nucleic acid encoding the mutant antibody according to
2 claim 1.
 - 1 5. The isolated nucleic acid according to claim 4, further comprising a
2 promoter operably linked to the nucleic acid sequence encoding the antibody.
 - 1 6. An expression vector comprising the nucleic acid according to claim 5.
 - 1 7. A host cell comprising the expression vector according to claim 6.
 - 1 8. The nucleic acid according to claim 4, comprising the sequence of
2 SEQ. ID NO 2 (FIG. 9).
 - 1 9. The nucleic acid according to claim 4, comprising SEQ.ID NO. 4
2 (FIG. 11).
 - sub 1
C4 2 10. A polypeptide comprising a peptide sequence according to SEQ. ID
2 NO.:5 (FIG. 11).
 - 1 11. A polypeptide comprising a peptide sequence according to SEQ. ID
2 NO.: 7 (FIG. 14).
 - 1 12. A nucleic acid encoding a polypeptide according to claim 14.
 - 1 13. A nucleic acid encoding a polypeptide according to claim 11.

1 14. The mutant antibody according to claim 1, wherein said mutant
2 antibody is mutant of CHA255.

1 15. The mutant antibody according to claim 14, wherein serine-95 of the
2 light-chain is substituted by a cysteine residue.

1 16. The mutant antibody according to claim 1, wherein said antibody is a
2 bifunctional antibody further comprising a second complementarity-determining region that
3 specifically binds to a cell-surface antigen.

1 17. The mutant antibody according to claim 1, further comprising a
2 targeting moiety covalently attached thereto.

1 18. The mutant antibody according to claim 17, having the structure:

Ab-L-T

wherein,

Ab represents said antibody;

L is a chemical bond or linking group that may contain one or more sites; and

T is said targeting moiety.

1 19. The mutant antibody according to claim 17, wherein said targeting
2 moiety is an antibody that binds specifically to a cell surface antigen.

1 20. The mutant antibody according to claim 1, further comprising said
2 metal chelate bound to said complementarity-determining region, wherein said chelate
3 comprises a reactive functional group of complementary reactivity to said reactive site of said
4 antibody.

1 21. The mutant antibody according to claim 20, further comprising a
2 covalent bond ~~between~~ formed by reaction of said reactive site of said antibody and said
3 reactive functional group of said chelate.

1 22. The mutant antibody according to claim 20, wherein said reactive site
2 of said chelate is an acrylamido moiety.

1 23. The mutant antibody according to claim 1, wherein said metal chelate
2 is a polyaminocarboxylate chelate of a metal ion selected from the group consisting of
3 transition metal ions and lanthanide ions.

1 24. A pharmaceutical composition comprising the mutant antibody
2 according to claim 17, and a pharmaceutically acceptable carrier.

1 25. A mutant antibody comprising a cysteine residue not present in the
2 wild-type of said antibody and a complementarity-determining region that specifically binds
3 to a metal chelate, wherein said cysteine is in a position proximate to or within said
4 complementarity-determining region.

1 26. An isolated nucleic acid encoding the mutant antibody according to
2 claim 25.

1 27. The isolated nucleic acid according to claim 26, further comprising
2 a promoter operably linked to the nucleic acid sequence encoding the antibody.

1 28. An expression vector comprising the nucleic acid according to
2 claim 26.

1 29. A host cell comprising the expression vector according to claim 28.

1 30. The antibody according to claim 25, wherein said antibody is a
2 bifunctional antibody further comprising a second complementarity-determining region that
3 specifically binds to a cell-surface antigen.

1 31. The mutant antibody according to claim 25, further comprising a
2 targeting moiety covalently attached thereto.

1 32. The mutant antibody according to claim 31, having the structure:

2 Ab-L-T

3 wherein,

4 Ab represents said antibody;

5 L is a chemical bond or linking group that may contain one or more functional
6 groups; and

7 T is said targeting moiety

1 33. The mutant antibody according to claim 31, wherein said targeting
2 moiety is a member selected from the group consisting of antibodies and antibody fragments,
3 each of which bind specifically to a cell surface antigen.

1 34. The mutant antibody according to claim 25, further comprising said
2 metal chelate bound to said complementarity-determining region, wherein said chelate
3 comprises a reactive functional group of complementary reactivity to the -SH side-chain of
4 said cysteine residue.

1 35. The mutant antibody according to claim 34, further comprising a
2 covalent bond formed by reaction of the -SH side-chain of cysteine and said reactive
3 functional group of said chelate.

1 36. The mutant antibody according to claim 35, wherein said reactive
2 functional group of said chelate is an acrylamido moiety.

1 37. The mutant antibody according to claim 25, wherein said metal chelate
2 is a polyaminocarboxylate chelate of a metal ion selected from the group consisting of
3 transition metal ions and lanthanide ions.

1 38. A pharmaceutical composition comprising the mutant antibody
2 according to claim 31, and a pharmaceutically acceptable carrier.

1 39. A method of treating a patient by administration of a metal chelate,
2 said method comprising the steps of :

- 3 (a) administering to said patient a pretargeting reagent;
4 (b) following step (a), administering to said patient a mutant antibody comprising;
5 (i) a complementarity-determining region that specifically binds to said metal
6 chelate;
7 (ii) a reactive site not present in the wild-type of said antibody and, wherein
8 said reactive site is in a position proximate to or within said
9 complementarity-determining region; and
10 (iii) a recognition moiety that binds specifically with said pretargeting moiety,
11 thereby forming a complex between said pretargeting reagent and said
12 mutant antibody; and

13 a (c) following step (b), administering to said patient said metal chelate, wherein said
14 chelate comprises a reactive functional group having a reactivity
15 complementary to the reactivity of said reactive site of said antibody, thereby;

16 (i) specifically binding said chelate to said complementarity-
17 determining region; and

18 a (ii) following step (i), forming a covalent bond between said mutant
19 antibody and said metal chelate through coupling the reactive
20 functional group of said chelate with said reactive site of said
21 mutant antibody.

1 40. The method according to claim 39, further comprising, between steps
2 (a) and (b), administering a clearing agent to said patient.

1 41. A method of treating a patient by administration of a metal chelate,
2 said method comprising the steps of :

3 (a) administering to said patient a mutant antibody comprising;

4 (i) a complementarity-determining region that specifically binds to said metal
5 chelate;

6 (ii) a reactive site not present in the wild-type of said antibody and, wherein
7 said reactive site is in a position proximate to or within said
8 complementarity-determining region; and

9 (iii) a targeting moiety that binds specifically to a cell by binding with a
10 member selected from the group consisting of cell surface receptors
11 and cell surface antigens, thereby forming a complex between said
12 mutant antibody and said cell; and

13 (b) following step (a) administering to said patient said metal chelate, wherein said
14 chelate comprises a reactive functional group having a reactivity
15 complementary to the reactivity of said reactive site of said antibody, thereby;

16 (i) specifically binding said chelate to said complementarity-
17 determining region; and

18 (ii) following step (i), forming a covalent bond between said mutant
19 antibody and said metal chelate through coupling the reactive
20 functional group of said chelate with said reactive site of said
21 mutant antibody.